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0933-0159P

IN THE U.S. PATENT AND TRADEMARK OFFICE

APPLICANT(S): Kalle SAKSELA et al. CONF: 9956
APPLICATION NO.: 09/579,894 GROUP: 1627
FILED: May 26, 2000 EXAMINER: B. Celsa
FOR: METHODS AND MATERIALS FOR GENERATING SH3
DOMAINS WITH TAILORED BINDING PROPERTIES

#17
Supp
11-19-02

PRELIMINARY RESPONSE UNDER 37 C.F.R. 1.114

Honorable Commissioner of Patents
Washington, D.C. 20231

November 6, 2002

Sir:

The following preliminary remarks are respectfully submitted.

REMARKS

In the Advisory Action of October 7, 2002 the Examiner refused entry of the September 6, 2002 amendment on the grounds that the amendments raised new issues for consideration. In the Advisory Action, the Examiner further indicated that, if entered, the September 6, 2002 response and amendments to claim 1 and 17-19 would overcome the indefinite rejections and new matter rejections. Applicants have separately requested entry of the September 6, 2002 amendment and Declaration of Dr. SAKSELA, upon refiling of the application.

The Examiner further indicates in the Advisory Action that the amendments and arguments of September 6, 2002 failed to overcome the rejections over the prior art because, the terms "artificial"; "randomization"; and "library" are used "in a manner neither supported by the specification nor recognized by the prior art." On this basis the Examiner asserts that the claims, as amended, are broad enough to encompass prior art embodiments. Applicants traverse this position of the Examiner and the rejection of the claims over the prior art and as being indefinite with regard to the recitation of "artificial"; "randomization"; and "library." These terms are well-known in the art and used with the same well-known meanings in the context of the present invention.

For example, attached hereto is an excerpt from a text book ("Genetic Engineering with PCR" Eds. M. Horton and R.C. Tait (1998)) wherein the term "random" is used as is commonly accepted in the art and as is intended with present claims. Chapter 12 of the Genetic Engineering with PCR text describes PCR-based methods of randomization, which are the same methods that have been used in the present specification for the randomization of the SH3 RT-loop region. Chapter 12 states in part,

Chapter 12: Beyond the Limits of Natural Diversity: PCR Synthesis of Semi-random Peptide and Antibody Phage Display Libraries

Proteins evolve naturally through mutation followed by selection for activities beneficial to normal function of organisms. Phage display of random peptide libraries allows the rapid *in vitro* evolution of polypeptides by selection of high-affinity variants

desirable for some artificial objective. While completely random pools of variant proteins might theoretically be an ideal starting point, experimental and biological limitations restrict the diversity of practical libraries. For this reason, randomization is often limited to only five or six codon positions. Although random pentamers and hexamers are useful for the mapping of continuous epitopes recognized by antibodies, these peptides are often too small to be used as ligands for most other proteins. For larger proteins, targeted mutagenesis and semi-random phage display libraries are often used to isolate variants with altered or improved specificity and affinity. These approaches are intermediate between random mutagenesis and rational design. Construction of semi-random libraries requires some a priori knowledge of the structural topology and binding domains of the target protein. Specific regions are targeted for randomization using mutagenic PCR primers. Internal random inserts are incorporated by PCR overlap extension and splicing. Several strategies are described for randomization using PCR templates. Specific examples of applications and the design of PCR primers and templates for the construction of semi-random peptide and antibody libraries are discussed. ("Genetic Engineering with PCR", Chapter 12, Eds. M. Horton and R.C. Tait (1998))

Regarding the term "library," attached hereto are two excerpts from dictionaries of genetic terms (Dictionary of Genetics (1985) and Oxford Dictionary of Biochemistry and Molecular Biology (1997)), wherein the term "library" is defined to have the same meaning as that of the invention.

Finally, regarding the term "artificial" a PubMed search of this term combined with the term "protein" results in 18,579 hits with these terms in the title, abstract or key word, and all of the hits that were reviewed used the term "artificial" as it is used with the present invention.

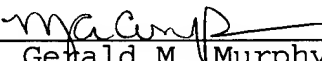
Thus, the present claims and all of the terms recited therein are common and well-known to those skilled in the art and the claims are fully compliant with the provisions of 35 U.S.C. §112, second paragraph. In addition, the claims when given their broadest reasonable interpretation would not encompass embodiments of the prior art. Issuance of the Notice of Allowance is therefore respectfully requested.

Should the Examiner have any questions regarding the present application she is requested to please contact MaryAnne Armstrong, PhD (Reg. No. 40,069) in the Washington DC area at (703) 205-8000.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §1.16 or under 37 C.F.R. §1.17; particularly, extension of time fees.

Respectfully submitted,

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